Claims

1. A method to prepare a nucleotide sequence encoding a modified PKS from a nucleotide sequence encoding a naturally occurring modular PKS wherein said naturally occurring modular PKS contains first regions which encode enzymatic activities and second regions which encode scaffolding amino acid sequences, which method comprises modifying at least one said first region.

2. The method of claim 1 wherein said modifying comprises deleting or inactivating at least one said first region.

3. The method of claim 1 wherein said modifying comprises replacing at least one said first region with a region encoding the corresponding enzymatic activity from a different naturally occurring PKS gene or from a different region of the same naturally occurring PKS gene.

4. The method of claim 1 wherein said nucleotide sequence encodes at least three PKS modules.

5. The method of claim 1 wherein said modifying results in utilization of a different extender unit.

6. The method of claim 1 wherein said modifying results in utilization of a different starter unit.

7. The method of claim 1 wherein said modification results in a polyketide of a different chain length.

8. A method to construct a library of colonies containing expression vectors for a multiplicity of different polyketide synthases which method comprises transforming recombinant host cells with a mixture of expression vectors containing the nucleotide sequences obtained by the method of claim 1; and

separating the transformed cells into individual colonies, and culturing the colonies.

9. A method to prepare a polyketide combinatorial library which method comprises culturing the library of colonies obtained by the method of claim 8 under conditions wherein said polyketides are produced.

10. A multiplicity of cell colonies comprising a library of colonies wherein each colony of the library contains an expression vector comprising a nucleotide sequence encoding a modular PKS derived from a naturally occurring PKS gene cluster wherein at least one enzymatic activity has been deleted and/or replaced by a different version of said activity or is mutated so as to result in a polyketide other than that produced by said naturally occurring PKS and

wherein the nucleotide sequence contained in each colony in the library encodes a different PKS.

11. The multiplicity of cell colonies of claim 10 wherein said naturally occurring PKS gene cluster is the erythromycin gene cluster.

12. The multiplicity of cell colonies of claim 10 wherein, in at least one colony of said library, said different version is the corresponding enzymatic activity from a different modular PKS or from another location in the same PKS gene cluster.

13. The multiplicity of cell colonies of claim 10 wherein the number of PKS modules contained in the expression vector is different in at least two colonies of the library.

14. The multiplicity of cell colonies of claim 10 wherein the extender unit utilized by the encoded PKS is different in at least two colonies of said library.

15. A method to produce a library of modular PKS proteins which method comprises culturing the multiplicity of cell colonies or the library of colonies of claim 10 under conditions wherein said expression vectors effect production of said modular PKS proteins.

16. A library of PKS proteins prepared by the method of claim 15.

17. A multiplicity of cell colonies comprising a library of colonies wherein each colony of the library contains a modular PKS derived from a naturally occurring PKS wherein at least one enzymatic activity has been deleted or replaced by a different version of said activity or is produced from a mutated form of said gene so as to result in a polyketide other than that produced by said naturally occurring PKS, and each colony in the library contains a different PKS.

18. The multiplicity of cell colonies of claim 17 wherein said naturally occurring PKS is the erythromycin PKS.

19. The multiplicity of claim 17 wherein the number of modules of PKS is different in at least two colonies of the library..

20. The multiplicity of claim 17 wherein the extender unit utilized by the PKS is different in at least two colonies of the library.

21. The multiplicity of claim 17 wherein the reduction cycle specificities are different in at least two colonies of said library.

22. A method to produce a combinatorial library of polyketides which method comprises culturing the cell colonies or library of colonies of claim 17 under conditions wherein polyketides whose synthesis is effected by said different PKS proteins are produced.

23. A combinatorial library of polyketides prepared by the method of claim 22.

24. A multiplicity of polyketides which comprises a combinatorial library of polyketides which results from culturing colonies containing polyketide synthases derived from a naturally occurring PKS wherein at least one enzymatic activity has been deleted and/or replaced by a different version of said activity or is mutated so as to result in a polyketide other than that produced by said naturally occurring PKS, wherein each PKS in said library produces a different polyketide.

25. The library of claim 24 wherein the chain length is different in at least two polyketides.

26. The library of claim 24 which contains at least two polyketides formed from different extender units.

27. The library of claim 24 which contains at least two polyketides of different oxidation states.

28. The library of claim 24 which contains at least two polyketides of differing stereochemistry.

29. The library of claim 24 which contains at least two polyketides formed from different starter units.

30. A method to identify a successful candidate polyketide which binds to or reacts with a target moiety, which method comprises screening the library of claim 24 by contacting each polyketide in said library with the target moiety under conditions wherein a successful candidate would form a complex with said target moiety, and

detecting any complex formed, thus identifying a polyketide of the library as the successful candidate.